Bio Science
CONTRACT PRODUCTION CORP.
BSCP

September 28, 1999

Dockets Management Branch (HFA09305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

[Docket No. 99D092013]

Provided below are comments on the Draft "Guidance for Industry: Cooperative Manufacturing Arrangements for Licensed Biologics".

Section VI. License requirement for a contract facility is unclear. The last sentence of the first paragraph states that a license is not required. However, in the second paragraph, there is a sentence that requires registration. (i.e. "Facilities performing contract operations for biological products must register with FDA in accordance with registration and listing provisions in 21 CFR part 207, 607, or 807.")

Section VI. In the second paragraph, please revise the sentence: "The contract manufacturer should also share with the applicant all important proposed changes ..." to:

- The contract manufacturer should also share with the applicant all important proposed changes to production and facilities (including introduction of new products) *that affect the applicant's process or license*; the license holder is responsible for reporting, as specified in 21 CFR 601.12, these changes to the FDA (See guidance documents entitled "Changes to an Approved Application: Biological Products: and "Changes to an Approved Application for Specified Biotechnology and Specified Synthetic Biological Products: dated July 1997).

Section VI. In the third paragraph, the contractor may subcontract testing with the approval of the license applicant. In that situation, the contractor is responsible for assuring compliance.

Section VI. Is CBER accepting Master Files such that contractors can protect the proprietary information for all contractors' license holders and clients?

Section VI. In the section on recommended written agreement between the applicant and the contractor please revise the seventh bullet to:

- A commitment from the contract facility to inform the license applicant of all *applicable* proposed changes in manufacture and facilities prior to implementation, including introduction of additional marketed products and clinical material processing operation, *(i.e. the types or categories)*

Section VI. In the section on recommended written agreement between the applicant and the contractor please revise the eighth bullet to:

- A commitment from the contract facility to fully inform the license applicant of all *applicable* errors and deviations in *the applicant's licensed* manufacturing methods and test results, as well as adverse events, for the affected product.

99D-2013 C2

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Section VI. Please add the following items to the recommended written agreement between the applicant and the contractor:

- A description (to include testing and responsibilities) of how raw materials will be released for use by the contract manufacturer
- A description of how process validation will be accomplished including responsibilities and written notification by both parties regarding changes
- A description of the manner and conditions of release of the API from the contract manufacturer
- A commitment from the license applicant not to request or require the contract facility to perform an operation or deviation that would jeopardize the compliance of the contractor
- A commitment from the license applicant to fully inform the contract facility of all processing, procedural or specification changes
- A commitment from the license applicant to complete necessary studies such as shipping validation, buffer stability studies and intermediate hold time studies

Since more companies are using cooperative manufacturing arrangements, this guidance will be beneficial. It is interesting that the guidance appears to be written to assist the license applicant, but does not provide assistance to the contract manufacturer who is trying to provide the best possible service to their clients. Please call me if you have any questions (410-563-9200, x249).

Sincerely,

Barbara B. Zinck
Vice President
Quality Assurance/ Regulatory Compliance

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